

REMARKS/ARGUMENTS

As the Examiner can see, Claims 1-7 and 12 were withdrawn from consideration, the Examiner previously rejected Claims 8-11 and 13. Claim 8 has now been amended, Claims 9 and 13 have been cancelled and thus, Claims 8, 10 and 11 are presented, in addition to new Claim 14.

Priority and Oath/Declaration Issues

Applicants acknowledge with appreciation that the Examiner deems the declaration previously submitted failed to claim foreign priority under Korean Application No. 10-2003-0002314. The Examiner indicated that such error can be corrected by supplying an Application Data Sheet in accordance with 37 CFR §1.76c. Applicants are investigating the present situation and will, if appropriate, submit such Application Data Sheet to ensure that appropriate foreign priority is set forth.

Rejection of Claims 8-11 and 13 Under 35 U.S.C. §112, Second Paragraph

The Examiner contends that Claim 8 is unclear with respect to the use of the term “semi-permeable agent”, with the Examiner indicating that particular listed agents are deemed materials that may or may not have permeability, with the Examiner asking for clarification thereof. The Examiner also has questions regarding the spatial relationship between scaffolds and the semi-permeable membranes; what the semi-permeable membranes are semi-permeable to; questions of whether proper antecedent basis for particular terms exist and makes suggestions with respect to a remedial recitation of language in the claim in order to make clear the recited steps carry out the intended method. Applicants acknowledge with appreciation the Examiner’s comments and have attended to suggested modifications of the claims in a manner believed to overcome the §112, second paragraph concerns. The Examiner’s favorable consideration is respectfully requested in this regard and a withdrawal of all §112 rejections of the above-referenced claims is therefore believed appropriate.

To further respond to the Examiner’s §112 concerns, Applicants submit the following:

The present invention relates to a method of preparing a biological tissue using scaffold pieces having a semi-permeable membrane on an overall outer surface thereof.

When the semi-permeable membrane is formed on the outer surface of the scaffold is seeded with tissue cells, nutrients are selectively introduced into the scaffolds from the outside, and metabolic wastes generated by the tissue cells are excreted to the outside of the scaffolds. The semi-permeable membrane is generated by the cross-linking of a semi-permeable agent, which is material for forming a hydro gel, such as alginates, polysaccharides, chitosan, agar powder and gelatin, with a cross-linking agent.

The examiner asserts that when a plurality of cell-seeded scaffolds are loaded into a single container, it would not appear that each of the scaffolds have an exposed surface to which a semi-permeable membrane can be applied. However, even if a plurality of cell-seeded scaffolds are loaded in a single container so that some of the scaffolds are in contact with each other, it does not matter the scaffolds are in contact each other because the semi-permeable membrane is formed on the overall outer surface of all the scaffolds in the container.

The container, in which a plurality of cell-seeded scaffolds are loaded, is normally packed with the semi-permeable agent, and the cross-linking agent is injected into the container such that it will diffuse over each scaffold covered with semi-permeable agent, thereby forming the semi-permeable membrane on the overall outer surface of all the scaffolds through the cross-linking of the semi-permeable agent and the cross-linking agent.

The scaffolds in the present invention are interconnected with the cross-linked semi-permeable membrane to make a single structure for a biological tissue. Also, since the semi-permeable agent of the present invention, such as alginates, polysaccharides, chitosan, agar powder and gelatin are soluble in the body, they should be cross-linked to prevent dissolution.

Rejection of Claim 13 Under 35 U.S.C. §102(e) as Being Anticipated by Bader

The Examiner rejects Claim 13, which the Examiner considers to be a product-by-process claim, on the disclosure made in Bader. Without conceding or agreeing with the Examiner's contentions, Applicants cancel Claim 13 without prejudice or disclaimer of the subject matter.

Rejection of Claim 13 Under 35 U.S.C. §102(e) as Being Anticipated by Zaleske et al.

The Examiner rejects Claim 13, again repeating that it is determined to be a product-by-process claim, in view of the disclosure of Zaleske et al. Without conceding to the Examiner's

position, Applicants cancel Claim 13 without prejudice or disclaimer of the subject matter thereof.

Rejection of Claims 8-11 and 13 Under 35 U.S.C. §103(a) as Being Unpatentable Over a Combination of Zaleske et al. and Bouhadir et al.

The Examiner admits that Zaleske et al. differ from the instant invention for, among other things, failing to teach the addition of a cross-linking agent. The Examiner contends, however, that, based on Bouhadir et al., use of calcium alginate gel as a biological gel and applying alginate and then calcium chloride according to Zaleske et al., would render the claimed invention obvious. The Examiner further bases his obviousness rejection on an alleged known substitution of Teflon for a Petri dish, arguing that such a substitution would yield the predictable result of successfully holding a construct, thereby allegedly rendering the claimed invention obvious to one of ordinary skill in the art. Applicants respectfully disagree with the Examiner's conclusion and traverse the Examiner's rejection of claims for the reasons as set forth below.

At the outset, Applicants have cancelled Claim 13 without prejudice or disclaimer of the subject matter thereof without conceding to the Examiner's basis for rejecting such claim as being obvious over a combination of Zaleske and Bouhadir et al. Independent Claim 8 has now been amended to further distinguish the present invention from the prior art and to provide further clarity to address the Examiner's §112, second paragraph concerns.

The determination of obviousness is made with respect to the subject matter as a whole, not separate pieces of the claim. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734 (2007); *Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1448 (Fed. Cir. 1984). Here, the application of hindsight is inappropriate where the prior art does not suggest the particular molding container having a predetermined size and form so that it is suitable to form the biological tissue being produced. The prior art can not be read as teaching or suggesting that one could reasonably be expected to manifest the claimed elements and properties. See, e.g. *Sanofi-Synthelabo, Sanofi-Synthelabo, Inc., V. Apotex, Inc.* (Fed. Cir. Dec. 12, 2008) citing *Graham*, 383 U.S. at 36 (cautioning against hindsight whereby the teachings of the invention are read into the prior art); see also *KSR v. Teleflexadvantages*, 127 S. Ct. at 1742 (recognizing "hindsight bias" and "ex post reasoning" as inappropriate in determination of obviousness). In *Graham v. John Deere Co.*, 383 U.S. 1 (1966) the Court recognized that the obviousness inquiry must

"guard against slipping into use of hindsight and to resist the temptation to read into the prior art the teachings of the invention in issue." *Id.* at 36.

Here, the Examiner has failed to set forth a *prima facie* case of obviousness as neither Zaleske et al. nor Bouhadir et al., even if combinable (which Applicants respectfully contend is not the case) would not have one of ordinary skill in the art at the time of the present invention, arrive at the presently claimed embodiments. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). No such desirability is suggested by the cited references.

All elements of the claim must be considered, rather than a more generalized recitation of what the invention comprises. *Aventis Pharma & King Pharma v. Lupin Ltd.* (Fed. Cir. 2007) (citing *KSR*) (one "must evaluate obviousness on a claim-by-claim basis.") The Examiner here seems to gloss over explicit limitations in the claims and instead attempts to support a combination of references by reciting broad principles not found in the claims. (e.g., neither reference discloses the precise process steps, such as the need for a molding container of a predetermined size suitable for forming the tissue being produced, etc.) The alleged teachings of a reference cannot be viewed in the abstract. Rather, they must be considered in the context of the teaching of the entire reference. See *Dembiczak*, 175 F.3d at 999. Care must be taken to avoid hindsight reconstruction while using the patent in suit as a guide through the maze of prior art references, combining just the right references in just the right way so as to achieve the result of the claims in suit. *Grain Processing Corp. v. American Maize Products Company*, 840 F.2d 902, 907, 5 USPQ 2d. 1788, 1792 (Fed. Cir. 1988). One cannot pick and choose individual elements from multiple references to recreate the invention. *Polaroid Corp. v. Eastman Kodak Co.*, 229 USPQ 561 (Fed. Cir.), cert. denied, 479 U.S. 850 (1996).

Any alleged showing of combinability must also be "clear and particular" and "supported by actual evidence." *Teleflex, Inc. v. Ficosa North Am. Corp.*, 299 F.3d 1313, 1334 (Fed. Cir. 2002). "[I]n each case the factual inquiry whether to combine references must be thorough and searching." *McGinley v. Franklin Sports*, 262 F.3d 1339, 1351-52 (Fed. Cir. 2001). Here, the Examiner has not carried her burden of establishing a *prima facie* case of obviousness because the prior art fails to suggest the desirability of the suggested combination. There is no actual evidence that one of skill in the art would make the combinations that Examiner has made, nor

any evidence that even if such combinations were made that the claimed invention would be the result thereof.

It is well established that an obviousness determination may not substitute the factual inquiry of whether to combine references must be thorough and searching. *In re Sang Su Lee*, 61 USPQ2d 1430 (Fed. Cir. 2002). It must be based on objective evidence of record. *Id.* Moreover, "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed." *In re Kotzab*, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); see also *KSR Int'l Co.*, 127 S. Ct. 1727, 1741 (2007) ("To facilitate review, this analysis should be made explicit.") (citing *Kahn*, 441 F.3d at 988).

Various embodiments of the present invention relate to the regeneration of biological tissues by preparing a porous scaffold, sectioning the scaffold into small pieces, seeding tissue cells onto the scaffold pieces, loading the scaffold pieces seeded with the tissue cells into a molding container of a predetermined form and size, forming a semi-permeable membrane on an overall surface of the scaffold pieces by a cross-linking procedure, and introducing nutrients into the scaffolds interconnected with the semi-permeable membrane.

Here, the molding container has a predetermined form and size for forming the biological tissue being produced. In contrast, Zaleske et al. (US Patent 6,183,737) is directed to using a sterile Petri dish.

New Claim 14 is fully supported by the specification and does not add any new matter. None of the prior art, alone or in combination, renders Claim 14 unpatentable.

Based upon the foregoing, Applicants believe that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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